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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,093	09/09/2003	John Daly	DAVI125.001CP1	9969
20995	7590	09/27/2005	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			MARVICH, MARIA	
2040 MAIN STREET			ART UNIT	
FOURTEENTH FLOOR			PAPER NUMBER	
IRVINE, CA 92614			1633	

DATE MAILED: 09/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/658,093

Applicant(s)

DALY, JOHN

Examiner

Maria B. Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25,27-44 and 46-145 is/are pending in the application.
- 4a) Of the above claim(s) 1-22,29,43,59-67,69-84 and 103-106 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-25,27,28,30-42,44,46-58,68,85-100 and 107-145 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This office action is in response to an amendment filed 8/8/05. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/8/05 has been entered. Claims 26, 45 and 101 have been cancelled. Claims 23, 93 and 94 have been amended. Claims 107-145 have been added. Claims 1-25, 27-44 and 46-145 are pending in this application. Claims 1-22, 29, 43, 59-67, 69-84 and 103-106 have been withdrawn. Therefore, claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are under examination in the application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23, 24, 27, 28, 30, 31, 33-42, 44, 46, 47, 50-58, 68, 85-9496, 97, 102, 107, 109-126 and 129-145 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. **This is a new rejection.**

During prosecution, claims must be interpreted as broadly as their terms reasonably allow. In the recited claims, only the polynucleotide encoding a polypeptide and the nucleic acid encoding the RNA element are in operable linkage otherwise, the broadest interpretation of a

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construct can be an organism or cell. Furthermore, as described below, the use of the term “half-life” is unclear. Numerous situations exist in which the half-life of a protein is very low such as in the liver or under degrading conditions. As well, an RNA element can be a polyadenylation sequence. Hence, given the broadest interpretation that can be given the claims, a construct need not be limited to a recombinant product but can be any product that comprises a polynucleotide that encodes a polypeptide with a half-life of less than 3 hours and comprises a polyadenylation sequence. In this instance, a construct can occur naturally. Therefore, the claims as written, do not sufficiently distinguish over constructs that exist naturally because the claims do not particularly point out any non-naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of “Isolated” or “Purified”

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection.**

Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are vague and indefinite in that the metes and bounds of “identifying elements of this type or agents that modulate their

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activity” are unclear. The terms “this type” and “their activity” are relative terms for which neither the specification nor the prior art prescribes a standard meaning. Therefore, it is unclear to what “this type” or “their activity” refer and the specification lacks the means to ascertain the meanings.

Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are vague and indefinite in that the metes and bounds of “half-life” are unclear. The specification teaches that the half-life can be “the time taken for half of the activity, amount or number of molecules to be eliminated”. The half-life is not just a property of the polypeptide but is also a property of the cell. Therefore, the half-life of a protein whether it be a measure of the activity or the amount or number of molecules, it is a relative term for which neither the specification nor the prior art provide a standard of ascertaining the requisite amount.

Claims 85, 91-95, 138, 144 and 145 are vague and indefinite in that the metes and bounds of “AU-rich element” are vague and indefinite. The term “rich” is a relative term for which neither the specification nor the prior art prescribes a standard meaning. Does an AU rich element require a minimum number of As and Us or is the presence of an A and a U sufficient. Furthermore, are other nucleotides tolerated or must the element be comprised of only As and Us.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85, 87-94, 96-100, 107-123, 135-138 and 140-145 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection.**

Applicants recite a construct that comprises a genus of RNA elements that modulate the stability of a transcript. However, applicants only disclose a species of RNA elements that are isolated from the 3'UTR of a variety of genes.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

In the instant case, applicants recite a construct for assaying the activity of a gene expression-modulating element or for identifying elements of this type or agents that modulate their activity. The construct comprises inoperable linkage a polynucleotide that encodes a polypeptide having an intracellular half-life of less than about 3 hours, a nucleic acid that encodes an RNA element that modulates the stability of a transcript encoded by the polynucleotide. The specification teaches that specific RNA elements are typically rich in the nucleotide bases AU and are found in the 3' UTR of a gene. Specifically, the specification

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teaches a variety of these genes and discloses several elements that function to modulate transcript stability such as from *c-fos* and found in SEQ ID NO:19. It is unclear if all 3' UTR sequences comprise the elements required to modulate stability or simply a subset of these genes such as those disclosed. While numerous RNA elements are found in nature, it is unclear whether any of these elements modulate stability as in the instantly recited claims. Neither the prior art nor the specification teaches that any of these elements mediate RNA stability. Given the large size and diverse nature of "RNA elements" and the inability to determine which will also possess the ability to modulate the stability of a transcript in a construct, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 68, 107-118, 120-122, 125, 126, 129-135, 138 and 140 are rejected under 35

U.S.C. 102(b) as being anticipated by Zhao et al (Methods in Enzymology, 1999, Vol 302, pages 32-38; see entire document) as evidenced by Eureka Bioscience (Eureka.com, Degradation of

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RNA in prokaryotes) further as evidenced by Kessler et al (NAR, 1986, p. 4939-4952; see entire document). **This is a new rejection.**

Zhao et al teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. page 33, paragraph 1) operably linked to a SV40 polyadenylation sequences, a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide (see e.g. figure 4). The polyadenylation sequence leads to destabilization of the transcript as evidenced by Eureka et al (see e.g. paragraph 1) as recited in claim 107. The components of the construct of Zhao et al are demonstrated in the instant specification to be functional in assaying the activity of a gene expression-modulating element as recited in claim 68 and 116. The polyadenylation sequence and the polynucleotide are heterologous to one another as recited in claim 108. The polynucleotide encodes a polypeptide that comprises GFP, which functions to emit light and as a selection marker, that is destabilized by introduction of the mouse ornithine decarboxylase degradation domain, and a PEST sequence, as recited in claims 109-113, 121, 125, 126 and 140. The construct comprises a *Bgl*III site in operable connection with the polynucleotide and the nucleic acid sequence (see e.g. page 34, paragraph 3, which describes insertion of NF-kB binding sites in frame with GFP at a *Nhe*I-*Bgl*III site) as recited in claim 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. figure 4) as recited in claim 117, 118 and 120. The vector is inserted into human cells (see e.g. page 35, paragraph 2) as recited in claims 133-135. The SV40 polyadenylation sequence comprises an AU rich element as evidenced by Kessler et al (see e.g. abstract) as recited in claims 138.

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Claims 68, 108, 109, 111-115, 117, 118, 120-122, 125, 126 and 129-133 are rejected under 35 U.S.C. 102(b) as being anticipated by Andersen et al (Applied and Environmental Microbiology, 1998, Vol 64, pages 2240-2246; see entire document) as evidenced by pUC18 map and Herrero et al (J Bacteriol, 1990, p. 6557-6567; see entire document). **This is a new rejection.**

Andersen et al teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. abstract) operably linked to transcriptional terminators, nucleic acid sequences that encode RNA elements that modulates the ability of a transcript encoded by the polynucleotide (see e.g. figure 1). The components of the construct of Andersen et al are demonstrated in the instant specification to be functional in assaying the activity of a gene-expression modulating element as recited in claim 68. The termination sequence and the polynucleotide are heterologous to one another as recited in claim 108. The polynucleotide encodes a polypeptide that comprises GFP, which functions to emit light and as a selection marker, and a destabilizing sequence, AANDENYALAA. The resulting polypeptide has a half-life of 40 minutes as recited in claims 109, 111-113 and 125. The construct further comprises a translational enhancer, RBSII, as recited in claims 119 and 121. The construct comprises a *NotI* and *SphI* site in operable connection with the polynucleotide and the nucleic acid sequence (see e.g. page figure 1C and table 1) into which is inserted a promoter and RBSII sites that enhance transcription and translation as recited in claim 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. figure 1b and as evidenced by the pUC18 map and Herrero et al, which describes pUC18Not as pUC 18 with a *NotI-EcoRI-SalI-HindIII-NotI* multiple cloning site) as

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recited in claim 117, 118 and 120. The vector is inserted into a cell (see e.g. page 35, paragraph 2) as recited in claims 133.

Claims 68, 93, 94, 96-100, 102, 107-118, 120-122, 125, 126, 129-136, 138 and 140-145 are rejected under 35 U.S.C. 102(a) as being anticipated by Leclerc et al (Biotechniques, 2000, Vol 29, pages 590-601; see entire document) as evidenced by Eureka Bioscience (Eureka.com, Degradation of RNA in prokaryotes) further as evidenced of Kessler et al (NAR, 1986, p. 4939-4952; see entire document) and further as evidenced by Clontech (pMAMneo map, downloaded 9/14/05). **This is a new rejection.**

Leclerc et al teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. abstract) operably linked to SV40 polyadenylation, a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide (see e.g. page 591, col 2, last paragraph as evidenced by the map for pMAM-neo). The components of the construct of LeClerc et al are demonstrated in the instant specification to be functional in assaying the activity of a gene-expression modulating element as recited in claim 68 and 116. The polyadenylation sequence leads to destabilization of the transcript as evidenced by Eureka et al (see e.g. paragraph 1) as recited in claim 107. The polyadenylation sequence and the polynucleotide are heterologous to one another as recited in claim 108. The polynucleotide encodes a polypeptide that comprises luciferase, which functions to emit light and as a selection marker, and the mouse ornithine decarboxylase degradation domain, which contains a PEST sequence (see e.g. page 590, col 2-3) as recited in claims 109-113, 121, 125, 126 and 140-143.

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The construct comprises a multiple cloning site in operable connection with the polynucleotide and the nucleic acid sequence (see e.g. map, pMAMneo) as recited in claim 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. map pMAMneo) as recited in claim 117, 118 and 120. The vector is inserted into a cell (see e.g. page 591, col 1, paragraph 2) as recited in claims 133-136. The SV40 polyadenylation sequence comprises an AU rich element as evidenced by Kessler et al (see e.g. abstract) as recited in claims 93, 94, 96-100, 102, 138, 144 and 145.

Claims 23-25, 27, 28, 30-37, 39-41, 46, 47, 50-55, 68, 85, 87, 107-118, 120-122, 125, 126, 129-134, 138 and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) as evidenced by Wach et al (Yeast, 1997, page 1065-1075; see entire document) as evidenced by Wach et al (Yeast, 1994, p. 1793-1808; see entire document) further as evidenced by Bennetzen and Hail, JBC, 1982, p. 30183025; see entire document) as evidenced by Eureka Bioscience (Eureka.com, Degradation of RNA in prokaryotes). **This is a new rejection.**

Mateus and Avery teach a construct comprising in operable linkage a polynucleotide that encodes a polypeptide have a half-life of less than about 3 hours (see e.g. abstract) operably linked to a nucleic acid sequence that encodes a RNA element that modulates the ability of a transcript encoded by the polynucleotide, ADH1 terminator. The construct does not contain a promoter but contain a multiple cloning site for insertion of gene expression modulating elements (see e.g. page 1314, col 2, last paragraph as evidenced by Wach et al, 1997, figure 4). The ADH1 is terminator encodes the polyadenylation sequence as evidenced by Wach et al

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(1994, page 1795, col 1, paragraph 3, which as evidenced by Eureka et al leads to destabilization of the transcript (see e.g. paragraph 1) as recited in claim 24, 35 and 107. As demonstrated in the instant specification, such a construct is functional in assaying the activity of a gene-expression modulating element as recited in claim 23, 68 and 116. The termination sequence and the polynucleotide are heterologous to one another as recited in claim 25 and 108. The polynucleotide encodes a polypeptide that comprises GFP, which functions to emit light and as a selection marker, and a PEST sequences at the C-terminus (see e.g. page 1314, col 2, last paragraph) as recited in claims 27, 28, 30-32, 46, 47, 87, 109-113, 121, 125, 126 and 140. The construct comprises a multiple cloning site in operable connection with the polynucleotide and the nucleic acid sequence for the insertion of promoter sequences or for linearization or for insertion of other elements (see e.g. page 1314, col 2, last paragraph as evidenced by Wach et al, 1997, figure 4) as recited in claim 33, 34, 41, 50-53, 114, 115, 122 and 129-132. The vector further comprises a selectable marker and an origin of replication (see e.g. Wach et al, figure 4) as recited in claim 36, 37, 40, 117, 118 and 120. The vector is inserted into a cell (see e.g. page 591, col 1, paragraph 2) as recited in claims 39, 54, 55, 133-134. As evidenced by Bennetzen et al. the termination sequence and polyadenylation sequence of ADH1 comprises an AU rich element (see e.g. figure 4) as recited in claim 85 and 138.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Li and Kain (US 6,130,313; see entire document). **This is a new rejection.**

Applicants claim a construct comprising a polynucleotide and a nucleic acid that encodes an RNA element that modulates stability of a transcript and a site for introducing a gene expression-modulating element and a translational enhancer in mammalian and human cells.

The teachings of Mateus and Avery are as above except:

Mateus and Avery do not teach that the methods of assaying promoters using a destabilized reporter can be used in human and mammalian cells.

Li and Kain et al teach methods of use of rapidly degrading GFP fusion constructs for use in analyzing regulatory elements and/or cis-acting regulatory elements. Li and Kain et al teach that these constructs comprise a GFP coding sequence fused to a mouse ornithine decarboxylase coding sequence in a vector. Li and Kain do not explicitly teach that the vectors lack promoters and comprise a sequence that encodes a RNA element that modulates the stability of the transcript.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the vector of Mateus and Avery in mammalian and human cells as taught by Li and Kain because Mateus and Avery, teach that it is within the ordinary skill of the art to generate a vector comprising GFP-pest for analysis of gene expression in cells and because Li and Kain teach that such a vector can be used in human and mammalian cells to analyze regulatory elements. One would have been motivated to do so in order to receive the expected

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benefit of promoterless vectors with destabilized transcripts and proteins to insert the regulatory elements to be examined as taught by Li and Kain. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 48, 49, 127 and 128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Methods in Enzymology, 1999, Vol 302, pages 32-38; see entire document) or Andersen et al (Applied and Environmental Microbiology, 1998, Vol 64, pages 2240-2246; see entire document) or Leclerc et al (Biotechniques, 2000, Vol 29, pages 590-601; see entire document) or Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Primig et al (Gene, 1998, Vol 215, pages 181-189; see entire document). **This is a new rejection.**

Applicants claim a construct comprising a chimeric gene comprising a coding sequence from a gene encoding a light emitting protein and a selectable marker protein and a nucleic acid sequence that encodes a RNA element that modulates the stability of a transcript encoded by the chimeric gene. The polypeptide encoded by the polynucleotide is a chimeric gene such as comprising genes encoding light emitting protein and a selectable marker protein.

The teachings of Zhao et al, Andersen et al, Leclerc et al and Mateus and Avery are described above and are applied as before except:

Neither Zhao et al, Andersen et al, Leclerc et al and Mateus nor Avery teach that the reporter is a chimeric gene encoding comprising genes encoding light emitting protein and a selectable marker protein.

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Primig et al teach use of a reporter gene that is a fusion between GFP and neomycin phosphotransferase (see e.g. page 183, bridging paragraph col 1-2). The cited benefits of the vector were localization of reporter and selection functions in one gene decreasing chances of undesirable recombination events, reducing false positives, optimal conditions for identifying gene expression modulators (see e.g. bridging paragraph page 187-188).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the separate reporter and selectable marker genes taught by Zhao et al, Andersen et al, Leclerc et al and Mateus and Avery with the GFP-neo fusion taught by Primig et al because Zhao et al, Andersen et al, Leclerc et al and Mateus and Avery teach that it is within the ordinary skill of the art to generate a vector comprising a destabilized reporter gene for analysis of gene expression in cells and because Primig et al teach that it is within the ordinary skill of the art to use GFP-neo as a reporter gene in cells. One would have been motivated to do so in order to receive the expected benefit of localization of reporter and selection function in one gene decreasing chances of undesirable recombination events, reducing false positives, optimal conditions for identifying gene expression modulators (see Primig et al, bridging paragraph page 187-188). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable Mateus and Avery (Yeast, 2000, Vol 16, pages 1313-1323; see entire document) in view of Svensson and Akusjarvi (EMBO J. 1985, Vol 4, No. 4, pages 957-964; see entire document). **This is a new rejection.**

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Applicants claim a construct comprising a polynucleotide and a nucleic acid that encodes an RNA element that modulates stability of a transcript and a site for introducing a gene expression-modulating element and a translational enhancer.

The teachings of Mateus and Avery are described above and are applied as before except:

Mateus and Avery do not teach that the vector further comprises a translational enhancer.

Svensson and Akusjarvi teach the use of adenovirus VA RNAI on the translation of mRNAs. The expression was elevated 2-6 fold (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add to the vector of Mateus and Avery, the VA RNAI translation enhancer taught by Svensson and Akusjarvi because Mateus and Avery, teach that it is within the ordinary skill of the art to generate a vector comprising a reporter gene for analysis of gene expression in cells and because Svensson and Akusjarvi teach that it is within the ordinary skill of the art to include a translational enhancer in a vector. One would have been motivated to do so in order to receive the expected benefit of enhanced reporter activity to identify low signaling events or elements that modulate these events. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Claims 23-25, 27, 28, 30-42, 44, 46-58, 68, 85-100 and 107-145 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 14, 2005

Maria B Marvich, PhD
Examiner
Art Unit 1633



DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER